



Abstract

## Protocol for the Systematic Review of the Biologic Pathways Linking Diet, Nutrition, and Physical Activity with Cancer: World Cancer Research Fund Global Cancer Update Project †

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Abstract: Background and Objectives: Biological and mechanistic data can support observational evidence to aid causal inference. The substantial body of available epidemiological evidence on the role of diet, nutrition, physical activity, and body weight and cancer has been systematically reviewed within the World Cancer Research Fund Global Cancer Update Program (WCRF CUP Global) over the past few decades. Mechanistic data can provide substantial additional support to established or suspected associations between diet and cancer but has not previously been systematically reviewed within the CUP Global. Here, we describe the development of a framework for the evaluation of biological and mechanistic data to support CUP Global in their evaluations. Methods: The protocol to evaluate mechanistic data utilizes a two-stage, iterative approach: (1) use of expert knowledge in combination with text mining automated tools (https://www.temmpo.org.uk/ accessed on 14 February 2024 to identify a set of the main potential mechanisms (typically 2-3 mechanisms) and their associated intermediate phenotypes (IPs) that link the factor of interest (exposure: E) to the cancer outcome of interest (outcome: O) and (2) for selected mechanisms, perform systematic literature reviews of human studies to evaluate the associations between E and IPs and between IPs and O. An expert committee then assesses the level of evidence for the role of each potential mechanism in the E-O association. If appropriate, additional literature reviews of experimental studies will be performed to address specific questions. Results: A protocol has been developed that can be used to systematically review data on mechanisms in a timely manner. As a first test case, the proposed protocol will be tested to evaluate mechanisms linking dietary patterns and colorectal cancer development. Discussion: This project will produce a framework for the systematic evaluation of mechanistic research to support causal associations between diet, nutrition, physical activity, body weight and cancer risk within WCRF CUP Global.

Keywords: protocol; biological pathways; mechanisms; cancer; nutrition



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